Remarks

Oath or Declaration:

The Action states that the declaration is defective for failing to identify the application by application number and filing date. Applicants respectfully disagree. The MPEP 602 VI. states that a declaration filed on the application filing date is acceptable if it contains:

(A) name of inventor(s), and reference to an attached specification which is both attached to the oath or declaration at the time of execution and submitted with the oath or declaration on filing;

(B) name of inventor(s), and attorney docket number which was on the specification as filed; or

(C) name of inventor(s), and title of the invention which was on the specification as filed.

The declaration was filed on the application filing date and included the names of the inventors, the title of the invention, and the attorney docket number, fulfilling both (B) and (C).

Objections to the claims:

Claims 6-9 have been objected to as being improperly dependent on claim 6. Applicants have amended the claims to make them dependent on claim 5.

Rejection of the claims under 35 USC §103:

Claims 5, 6, and 9 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Wolff et al. (U.S. Patent 5,744,335) in view of Wolfert et al (Bioconjugate Chem. 1999). It is the Applicants' opinion that histone and polyvinylamine can not be considered to be structurally close and of common utility. Histone, taught by '335, is a naturally occurring protein having a three-dimensional structure that is explicitly "designed" to bind to genomic DNA. The protein contains cationic, anionic and hydrophobic groups. In contrast, polyvinylamine is a synthetic cationic polymer lacking anionic or hydrobhobic groups. While both molecules may reasonably be expected to associate ionically with nucleic acids of all sorts, they can not be reasonably be anticipated to interact with both large plasmids DNAs (supercoiled nucleic acid several thousand base pairs in length) and oligonucleotides (less than 30 base pairs) in a way that facilitates delivery to cells. Further, there is no evidence in the prior art to suggest than both a DNA binding protein, such as histone, and a synthetic

polycation, such as polyvinylamine, would combine with an amphipathic compound to make an effective oligonucleotide (such as siRNA) transfection reagent.

While Wolfert et al. do in fact teach that cationic polymers such as polyvinylamine efficiently condense DNA (as the prior Action states), Wolfert et al. do **not** teach that all cationic polymers, and in particular polyvinylamines, make good nucleic acid delivery agents. On page 999, 1st column, 3rd paragraph, Wolfert et al. state "However, pVA.HCl/DNA complexes tended to flocculate in water, particularly with lower molecular weight pVA.HCl, and no AFM images were possible." Flocculation of complexes can be expected to inhibit nucleic acid delivery to cells and Wolfert et al. note that polyvinylamine "gave no significant spontaneous transfection when applied to 293 cells in vitro" (page 999, 2nd column, 2nd paragraph). Further, on page 999, 2nd column, 3rd paragraph, Wolfert et al. teach that "Following direct inoculation into Xenopus oocytes, complexes based on most homopolymers produced levels of gene expression comparable to that following injection of free DNA." However, "pAA.HCl and pVA.HCl complexes showed over 60% expression." This results means that, compared to other homopolymers, pAA and pVA caused a **reduction** in transcription ability of the associated DNA. Thus, if direct injection of complexes into Xenopus oocytes is to be considered in vivo, then Wolfert et al. teach that polyvinylamined inhibit DNA delivery. Further, Wolfert et al. provide no teaching or suggestion on how any polymers will interact with oligonucleotides, such as siRNA, or with amphipathic compounds to delivery an oligonucleotide to a cell in vivo or in vitro. Applicants request reconsideration of the rejection.

Rejection of the claims under 35 USC §103:

Claims 5, 6, and 9 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Wolff et al. (U.S. Patent 5,744,335) in view of Meier et al. (U.S. Patent 6,616,946). Applicants respectfully disagree. Meier et al. describe the formation of polymeric hollow particles with variable permeability for encapsulating active agents. Neither Wolff et al. nor the instant application teach formation of a hollow particle. Therefore, it would not have been obvious to combine a polymer potentially useful in forming a polymeric hollow particle with the teaching of Wolff et al.

As further evidence that the combination of a polyvinylamine with the teaching of Wolff et al. would not have been obvious in the development of an siRNA delivery agent, Applicants provide the attached Declaration under 37 CFR 1.132. The declaration shows that the replacement of histone with polyvinylamine in the teaching of Wolff et al. does not provide an effective DNA delivery agent. Delivery of DNA to either 3T3 cells or CHO cells using polyvinylamine (pVA) + lipid + DNA was no more effective than using DNA alone. In contrast, histone + lipid + DNA resulted in high levels of plasmid delivery as evidenced by luciferase transcription as measured by relative light units.

The Examiner's rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendment and arguments, it is submitted that claims 1-3 and 5-9 should be allowable.

Respectfully submitted,

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I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as express mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this date: December 11, 2006 .

/Kirk Ekena/
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